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Aortic Elastic Properties in Patients With Coronary Artery Ectasia

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Background The purpose of the present study was to investigate the elastic characteristics of the aorta in patients with coronary ectasia (CE) and the relationship between these characteristics and echocardiographic left ventricular (LV) diastolic functions.

Methods and Results In the first group there were 35 patients with CE, the second group consisted of 35 patients with coronary artery disease (CAD) and the third group consisted of 35 patients with normal coronary arteries. Echocardiographic investigation was carried out for the assessment of the LV diastolic functions. Aortic strain, β index and aortic distensibility were used as aortic elasticity parameters. LV diastolic functions were impaired in both the ectasia group and the CAD group as compared with patients with normal coronary arteries. Beta index and aortic distensibility measurements were similar between the CAD and CE groups. The values obtained for aortic strain, β index and aortic distensibility were lower in the CAD and ectasia groups when compared with the values of the normal group. On performing the stepwise linear multivariable analyses, aortic elastic parameters have been determined to possess the strongest diagnostic power for LV diastolic functions.

Conclusions The results of the current study show that stiffness parameters of aorta are impaired in the patients with CE as in the patients with CAD. The increase in aortic stiffness might be responsible for LV diastolic dysfunction. (*Circ J* 2007; **71:** 506–510)

Key Words: Arterial stiffness; Coronary artery disease; Coronary ectasia; Diastolic dysfunction; Left ventricular function

Coronary ectasia (CE) is a clinical situation which is characterized by luminal widening of the coronary arteries and the resultant decrease in the coronary blood flow. Its incidence has been reported to be between 0.3% and 4.9% in the autopsy and cardiac catheterization series[1] Coronary atherosclerosis (50%), congenital diseases (20%), inflammatory diseases (10–20%), collagenous and connective tissue diseases are presumed to be responsible for its cause[2] The essential histopathological finding in the diagnosis of CE is the replacement of coronary artery media layer smooth muscle cells with hyalinized collagen, as a consequence of the increased degeneration of the media layer[3] As a result, the loss of musculo-elastic components is observed in the media[2] Thus, progressive artery dilatation occurs. Moreover, along with this disease, the presence of extracardiac artery dilatation has been reported in the previous studies[4,5]

Arterial stiffness, which is defined as the arterial rigidity caused by the loss of elastic tissue in the artery wall, decreases the widening capacity of the artery. Many studies searching the effects of the cardiovascular risk factors on the arteries showed that, as a consequence of the structural changes in the arteries caused by these risk factors, arterial rigidity develops and arterial widening capacity is deteriorated. It has been established that as the stiffness of the large arteries such as aorta increases, cardiovascular mortality and morbidity also increase[6] Consequently, aortic stiffness has recently been regarded as a risk factor that needs to be treated[7] It has also been established that aortic stiffness is increased in individuals with coronary artery disease (CAD) and in those with atherosclerosis and that it is an independent predictor of CAD[8] In the present study, we reported that there might possibly be a relationship between the increment in aortic stiffness and left ventricular (LV) diastolic dysfunction[9]

In the current study our objective was to investigate the elastic properties of the aorta in the patients with CE and the relationship between these characteristics and LV diastolic functions.

Methods

Study Population

The cases were selected from the patients who admitted to our cardiology department for coronary angiography between the years 2001 and 2004. The study population was divided into 3 groups according to the results of the coronary angiograms. A total of 105 patients were enrolled in the present study; in the first group there were 35 patients with CE, the second group consisted of 35 patients with CAD (coronary lesion causing ≥50% luminal narrowing in at least 1 coronary artery) and the third group consisted of 35 patients with normal coronary arteries. CE was defined as localized or diffuse non-obstructive lesions of the epicardial

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coronary arteries with luminal dilatation exceeding the 1.5-fold of normal adjacent segment![10] When there was no identifiable adjacent normal segment, the mean diameter of the corresponding coronary segment in the control group served as the normal values. The average diameter of ectatic segments was determined by adding the maximal diameters of all ectatic segments and then dividing the obtained value by the number of ectatic segments. Diagnostic echocardiographic study was carried out for all the patients. Before the echocardiographic study, each patient completed a questionnaire about medical and disease history and current medications. Furthermore, all participants underwent a routine cardiological evaluation (blood pressure (BP) measurement, electrocardiogram). Supine systolic and diastolic BP (SBP/DBP) was measured after at least 10 min of undisturbed rest with the cuff method. Hypertension was defined as having SBP value ≥140 mmHg and/or diastolic pressure value ≥90 mmHg or using antihypertensive medication. Doppler echocardiography was carried out for each patient after the routine cardiological assessment. Both the sonographer and the reporting cardiologists were blinded to the patients' angiographical findings. The study was approved by our local ethic's committee and written informed consent was obtained from each participant.

Exclusion Criteria

Exclusion criteria were as follows: (1) acute coronary syndrome, a previous myocardial infarction and congestive heart failure; (2) valvulopathy, persistent atrial fibrillation, congenital heart disease; (3) diabetes and dyslipidemia; and (4) chronic severe alcoholism.

Echocardiographic Measurements

All the measurements were carried out while the subjects were in the left lateral decubitus position by M mode, 2-dimensional and Doppler echocardiography. Vivid 5 Doppler echocardiographic unit (GE Vingmed Ultrasound, Horten, Norway) with 2.5 MHz probe was used. Echocardiographic tracings were recorded on super VHS videotapes at a sweep speed of 50 mm/s. The basic measurements of LV dimensions in diastole and systole, thickness of interventricular septum and posterior wall were measured by the M-mode technique. LV mass (LVM) was calculated by using the Devereux's formula:[11]

$$\text{LVM} = 0.8 \times [1.04 \times (\text{septal thickness} + \text{posterior wall thickness} + \text{LV end diastolic diameter})^3 - (\text{LV end diastolic diameter})^3] + 0.6\ \text{g}.$$

LVM was then divided by body surface area to obtain LVM index (LVMI). The LV diameters, volumes and systolic functions were measured according to the recommendations of the American Society of Echocardiography![12] LV ejection fraction (LVEF) was calculated as (diastolic volume-systolic volume)/(diastolic volume) by Simpson's method. Early (E) and atrial (A) transmitral maximal flow velocities, the E/A ratio, deceleration time (DT) of E wave and isovolumic relaxation time (IVRT) were registered. The following measurements were obtained for the determination of myocardial diastolic function by pulsed Doppler tissue imaging (DTI). Pulsed DTI of the LV basal inferior wall was carried out in the apical 2-chamber view. Early (Em) and atrial (Am) diastolic waves (cm/s), peak velocity of myocardial systolic wave (Sm) (cm/s), Em/Am ratio, Em-wave DT (DTm in ms) were measured. The pulmonary venous flow parameters were defined as follows: S-wave, peak systolic flow velocity in the pulmonary vein; D-wave, peak diastolic flow velocity in the pulmonary vein; and duration of pulmonary-atrial reversal signal. Diastolic function of the left ventricle was defined by 4 patterns: normal, abnormal relaxation pattern, pseudonormal pattern and restrictive filling pattern.

The aortic diameter was recorded at a level 3 cm above the aortic valve by M-mode echocardiography![13] Internal aortic diameters were measured by means of a caliper in systole and diastole as the distance between the trailing edge of the anterior aortic wall and the leading edge of the posterior aortic wall. Aortic systolic (AoS) diameter was measured at the time of full opening of the aortic valve and diastolic (AoD) diameter was measured at the peak of QRS. Ten consecutive beats were measured routinely and averaged. The AoS and AoD indexes for each participant were calculated by dividing the AoS and AoD by the body surface area. The percentage change of the aortic root was calculated as:

$$\%\text{Ao} = 100 \times (\text{AoS} - \text{AoD})/\text{AoD}$$

to obtain the aortic strain. All recordings were analyzed by the same investigator blinded to the patients' categories. A second analysis of the video recordings of the echocardiographic examinations was carried out within 1 week by the same echocardiographer using the Vingmed analysis software to minimize intraobserver variability. Intraobserver variability was minimal (coefficient of variation for echocardiographic parameters ranged from 7% to 9%).

BP

The BP measurements of all the patients were carried out while they were in the supine position with a mercury sphygmomanometer. Korotkoff phases I and V were used to determine the systolic and diastolic pressures respectively, and the average of 3 readings were regarded as the clinical BP. Pulse pressure (PP) value was obtained by subtracting DBP value from systolic pressure value, and the following indexes of the elastic properties of the aorta were calculated: (1) aortic root distensibility $= 2 \times (\text{AoS} - \text{AoD})/\text{PP} \times \text{AoD}$, in $\text{cm}^2\ \text{dynes}^{-1}$ and (2) β index $= \ln(\text{SBP}/\text{DBP})/\text{aortic strain}$![14–16] LV meridional systolic wall stress was estimated by modifying previously published methods assuming that LV geometry is spherical and wall thickness is uniform![17] The following formula was used for this measurement: end-systolic wall stress $(\text{kdyne}/\text{cm}^2) = 0.334 \times \text{SBP} \times \text{LVDS}/[\text{PWS} \times (1 + \text{PWS}/\text{LVDS})]$; where LVDS is systolic LV diameter and PWS is systolic posterior wall thickness.

Statistical Analysis

Numerical variables were expressed as the mean ± SD. All the numerical variables of the study groups presented a normal distiribution and the variances between the groups were equal. Thus, one-way ANOVA for mean and post-hoc Tukey test were used for individual group differences for the comparison of groups. Linear correlation analysis with Pearson's coefficients was used to assess the strength of association between variables. Stepwise linear regression analyses, which was carried out by parameters that showed significant correlation in univariate analysis was used for determining diagnostics of LV diastolic function parameters. Statistics were calculated with SPSS 11.0 statistical package program. A p-value of <0.05 was accepted as statistically significant.

Table 1 Comparison Between Groups

	CE patient (n=35)	CAD patients (n=35)	Controls (n=35)	p value
Demographic charecteristics				
Age (years)	58±10	60±9	60±7	NS
Gender (M/F)	19/16	20/15	17/18	NS
Smoking (%)	8	11	8	NS
Hypertension (%)	54	48	54	NS
Weight (kg)	81±18	83±15	80±11	NS
Height (cm)	1.68±0.18	1.67±0.15	1.69±0.14	NS
BMI (kg/m^2)	28.7±5	29.8±5	28.1±4	NS
SBP (mmHg)	128±10	117±12	125±11	NS
DBP (mmHg)	82±6	71±5	78±8	NS
Heart rate (pulse/min)	71±4	66±4	67±6	NS
Echocardiographic parameters				
IVS diastolic thickness (cm)	1.02±0.12	1.01±0.11	0.98±0.15	NS
PW diastolic thickness (cm)	0.9±0.07	0.91±0.13	0.88±0.17	NS
LV diastolic diameter (cm)	5.11±0.57	5.14±0.42	4.96±0.35	NS
LV systolic diameter (cm)	3.38±0.38	3.26±0.46	3.16±0.36	NS
LV mass index (g/m^2)	96.7±18.4	94.3±18.7	91.3±15.7	NS
LV ejection fraction (%)	65.3±5.2	65.9±8.4	68.4±7.2	NS
Doppler parameters				
Diastolic dysfunction (+/–)	25/10	22/13	4/31	0.0001*
Peak E/A ratio	0.76±0.04	0.93±0.03	1.10±0.03	<0.05
DT (ms)	272±12	230±6	194±6	<0.05
IVRT (ms)	148±5	121±6	104±3	<0.05
Em/Am ratio	0.67±0.04	0.76±0.05	1.23±0.59	<0.05
Aortic elasti c parameters				
Systolic diameter (cm)	3.1±0.08	2.9±0.07	2.8±0.06	<0.05*
Diastolic diameter (cm)	2.9±0.07	2.7±0.06	2.6±0.06	<0.05*
Strain (%)	7.1±0.4	9.4±0.7	13.2±0.8	0.01
β index	1.46±0.06	1.61±0.09	2.03±0.08	0.001*
Distensibility (cm^2·dyn^{-1}·10^{-6})	3.2±0.2	4.2±0.4	6.1±0.4	0.001*
End-systolic wall stress (kdyne/cm^2)	54.7±11.8	52.5±9.6	42.6±7.7	0.027*

CE, coronary ectasia; CAD, coronary artery disease; BMI, body mass index; SBP, systolic blood pessure; DBP, diastolic blood pressure; IVS, interventricular septum; PW, posterior wall; LV, left ventricular; E/A, mitral early diastolic flow velocity/late diastolic flow velocity; DT, deceleration time of E wave; IVRT, LV isovolumic relaxation time; Em, early myocardial Doppler peak velocity; Am, late myocardial Doppler peak velocity.
**Control vs CE and CAD groups.*

Table 2 The Properties of Ectasia in the Patients With CE

Average diameter of ectasia (mm), (mean±SD)	5.35±0.72
Number of ectasic segments (mean±SD)	3.3±1.1
Distribution of ectasic segments	
1 segment	3/35 (9%)
2 segment	8/35 (23%)
3 segment	10/35 (28%)
4 segment	6/35 (17%)
5 segment	6/35 (17%)
6 segment	2/35 (6%)
Distribution of coronary artery ectasia	
1 vessel ectasia	5/35 (14%)
2 vessel ectasia	10/35 (29%)
3 vessel ectasia	20/35 (57%)

Abbreviation see in Table 1.

Results

Clinical Characteristics of the Patients

The study population consisted of 105 patients (56 male and 49 female). The average age was 59.5±9 years. There were no differences between the groups in terms of age, gender, BP values or smoking status. Demographic and clinical characteristics of the patients are presented in Table 1.

Echocardiographic Parameters

Table 1 outlines the echocardiographic data of the groups. Analysis of the values of the 105 patients showed that LVMI and LVEF were similar between the groups. LV diastolic dysfunction was present in 25 of the 35 CE patients, in 22 of the 35 CAD patients and in 4 of the 35 control subjects. Impaired relaxation was by far the most common abnormal pattern in the groups (17, 14 and 4 patients, respectively). Pseudonormal pattern was observed in 7 of the CE patients and in 8 of the CAD patients. Restrictive filling pattern was documented in only 1 patient of all the patients with CE. LV diastolic parameters were also compared and the patients with CE and CAD were observed to have worsened diastolic parameters than the control subjects (Table 2). The E/A ratio was lower in the CE and CAD groups as compared with the control group (CAD vs CE p=0.01; CE vs control p=0.001; CAD vs control p=0.03). The DT values were found to be the longest in the CE group, and the shortest in the control group (CAD vs CE p=0.01; CE vs control p=0.001; CAD vs control p=0.01). Seemly, IVRT was found to be significantly higher in the CE group when compared with CAD and control groups (CAD vs CE p=0.01; CE vs control p=0.001; CAD vs control p=0.03). The E/A and Em/Am ratio were significantly correlated with the aortic distensibility (r=0.42, p=0.001; r=0.34, p=0.005).

Existing data show that, LV diastolic functions of the patients in the CE group are impaired as they are in the CAD group. The E wave velocity is found to be low only in the CE group, suggesting a much earlier development of

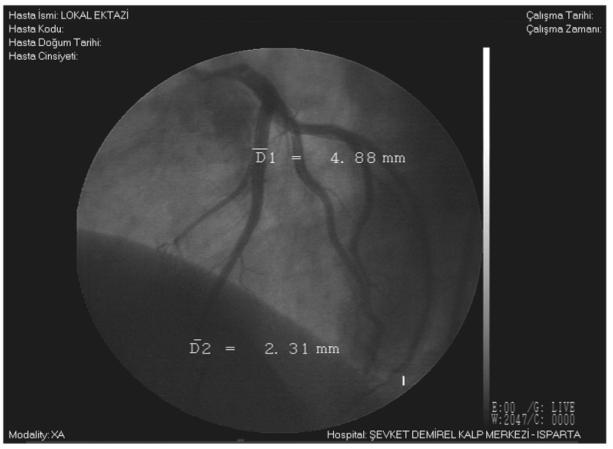

Fig 1. An example of the coronary angiographical views of a patient with coronary ectasia.

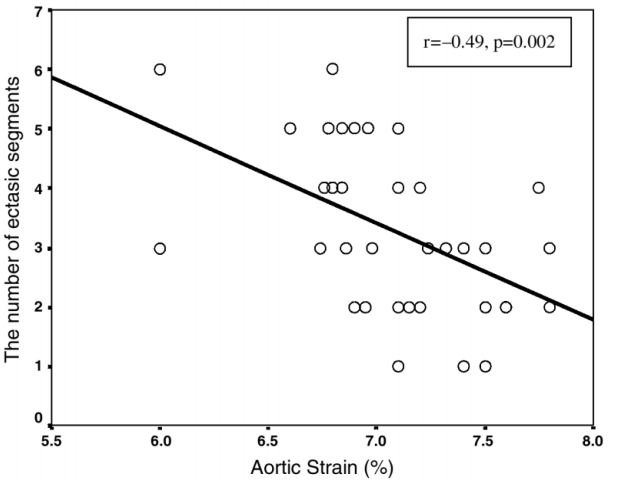

Fig 2. Correlation between the aortic strain and the number of ectasic segments.

impairment in this group when compared with the CAD group.

An example of the coronary angiographical views of a patient with CE is shown in Fig 1. Table 2 shows the properties of the ectatic vessels of the CE patients. One vessel, 2 vessel and 3 vessel ectasia were found to be present in 5 (14%), 10 (29%) and 20 (57%) patients respectively. We found a negative correlation between the number of ectatic segments and distensibility (r=–0.35, p=0.005), strain (r=–0.49, p=0.002, Fig 2) and tissue Doppler Em/Am ratio (r=–0.31, p=0.03) in the correlation analyses.

Elasticity Parameters of the Aorta

Aortic strain, aortic distensibility and index values, which are the elasticity parameters of the aorta, were found to be lower in the CE and CAD groups as compared with the values of the control group. However, while index and aortic distensibility measurements were similar between CAD and CE groups, the aortic strain was found to be lower in the CE group. LV end-systolic wall stress was significantly greater in the CE and CAD patients than the normal controls. Aortic elasticity parameters are presented in Table 1.

The stepwise linear multivariable analyses showed that aortic elasticity parameters have the strongest diagnostic power for the detection of the abnormalities in the LV diastolic function. Among these parameters, the aortic strain has been found to possess the strongest diagnostic power for E/A rate, DT and IVRT (r=0.46; p=0.001, r=0.37; p=0.01 and r=0.41; p =0.01, respectively).

Discussion

LV diastolic function disorder can be defined as delayed filling of the ventricle, which causes an increase in the left atrial pressure with time as a compensatory mechanism. Besides diastolic dysfunction, LV filling obstructions and impaired LV compliance might cause LV systolic dysfunction. LV diastolic dysfunction is very important because it might play a key role in the development of cardiac failure and it may be the only finding in the early stages of various heart diseases such as CAD, hypertension, constrictive pericarditis, restrictive or hypertrophic cardiomyopathy. Doppler is the most frequently applied method in the diagnosis of LV diastolic dysfunction.

In the current study, a relationship between LV diastolic functions and aortic stiffness has been shown. The precedence of impairment of diastolic functions and the subsequent impairment of systolic functions are already known. Increased aortic stiffness also contributes to this situation. In the previous studies the relationship between aortic stiffness and the myocardial mass and functions has been presented[9,18] Some structural changes occur in the myocardium when the end-systolic stress increases. Thus, systolic and diastolic stiffness develops in the myocardium[19] However the systolic function is preserved, while the diastolic function is impaired at the first stage of these compensatory changes[19] Systolic function is impaired in the later stages. Besides the ventricular geometry, aortic functions are also presumed to be responsible for the end systolic stress[9,18] Increased stiffness can be a potential factor for wall stress. When afterload is increased, elevated intraventricular pressure has to be generated first to open the aortic valve, and then during the ejection phase these increases in afterload and intraventricular pressure lead to an increase in myocardial wall stress. In animal models, loss of aortic distensibility directly affects the mechanical performance of the left ventricle, with increases noted in LV systolic pressure and wall tension[20]

In the current study, we observed that the impairment of LV diastolic function in the patients with CAD was more than that of the patients with normal coronaries. Similarly, LV diastolic function impairment in the patients with CE might be explained by the above-mentioned hypothesis. Moreover, aortic elasticity parameters are the strongest diagnostic parameters for LV diastolic functions and this also supports this hypothesis.

As far as we know, tissue Doppler examination is better than conventional Doppler in the assessment of diastolic functions[21] Therefore, tissue Doppler method was used in the present study for the assessment of LV diastolic functions. Tissue Doppler results were found to be correlated with the conventional Doppler results in our study, which was concordant with the results of the previous studies.

Arterial stiffness is known as the arterial rigidity that develops because of the loss of elastic tissue in the arterial wall, resulting in the loss of widening capacity of the artery. It has been reported that, cardiovascular mortality

and morbidity rates increase with the increase of the stiffness in the large arteries[9]. Therefore, aortic stiffness has recently been regarded as a risk factor which needs to be treated.

Such an evidence does not exist regarding CE which shares the same physiopathology with CAD. In the current study it seems that, similar to CAD patients, these stiffness parameters of aorta are also impaired in the patients with CE. Furthermore, the impairment in the CE group was more than that observed in the CAD group. This indicates that the destruction of the arterial media layer is greater in case of CE, which results in a much higher increment in aortic stiffness. Similarly, the detection of much higher systolic and diastolic aortic diameter values in patients with CAD and CE compared with patients with normal coronaries, also supports this. This increase was found to be higher in patients with CE when compared with patients with CAD. The concept that has been reported in the previous studies indicating that extracardiac constraint might appear in patients with CE, also supports the above point of view. The increase of aortic stiffness in the patients with CE shows that, CE might not just be an innocent widening. However, more data regarding this issue are needed.

Conclusion

Aortic stiffness is observed to increase in the patients with CAD and CE. This result supports that, CE is a generalized vascular disorder rather than a microvascular disease process. The increase in aortic stiffness might be responsible from LV diastolic dysfunction. The assessment of the aortic properties and the LV functions of the patients with CE is important regarding the timing of treatment. It is also important to perform new studies to follow up these patients in terms of observing the progression of the impairment of aortic elastic parameters and LV function.

Study Limitations

The major limitations of the current study are the small sample size and the possible underestimation of the presence of atherosclerotic plaque with coronary angiography. Even though the study groups were small they were quite homogeneous. Intravascular ultrasound might have overcome the limitation of angiography with tomographic images, which provides accurate characterization of vessel lumen and wall geometry, as well as the presence and distribution of atherosclerosis.

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